

## **EXHIBIT A**

**PATENT**

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

**In re Application of:**

John A. Schillinger *et al.*

Serial No.: 10/052,771

Filed: July 7, 2006

For: PLANTS HAVING RESISTANCE TO  
MULTIPLE HERBICIDES AND ITS USE

Group Art Unit: 1661

Examiner: David H. Kruse

Atty. Dkt. No.: ASGR:002USDI  
11000023-0006

**DECLARATION OF PAUL FENG UNDER 37 C.F.R. § 1.132**

I, Paul Feng, hereby declare as follows:

1. I am a U.S. citizen and currently reside in Wildwood, Missouri.
2. I have been employed by Monsanto Company since 1981, currently with the title of Senior Science Fellow.
3. I hold a Ph.D. in Biochemistry from North Dakota State University and a B.S. in Biology from the University of North Dakota. I have been conducting research in the area of agricultural biotechnology since 1981. My duties have included the development of transgenic crop technologies.
4. I am familiar with the contents of the above-captioned patent application, which I understand has an earliest claimed filing date of March 7, 1997.
5. I understand that the Patent and Trademark Office Examiner in charge of assessing the patentability of the above-captioned patent application has rejected the patent application

as being obvious over Barry *et al.* (U.S. Patent No. 5,463,175) in view of Strauch *et al.* (U.S. Patent No. 5,276,268) and Kishore *et al.* (U.S. Patent 5,312,910) and in further view of Shah *et al.* (U.S. Patent No. 5,188,642). In particular, I understand that the Examiner rejected the claims based on the assertion that Barry *et al.* discloses, at Example 5, the introduction of a transgene encoding glyphosate oxidase (GOX) and a transgene encoding a sulfonylurea-resistant form of the maize acetolactate synthase gene (ALS) into Black Mexican Sweet (BMS) corn cells.

6. A person of ordinary skill in the field of agricultural biotechnology as of March, 1997 would not have understood Barry *et al.*, particularly Example 5, to teach or suggest the production of a soybean plant or seed comprising transgenes for both glyphosate resistance and sulfonylurea resistance. This is because Barry *et al.* clearly were using the corn ALS gene on the EC9 plasmid only to select transformed cells, in a selection procedure that was used at that time to obtain transgenic plants for a gene of interest on a plasmid that is co-transformed with the EC9 plasmid, *e.g.*, as practiced by Barry *et al.* There, the gene of interest is the co-transformed gene, the GOX gene, and not the ALS gene. Additionally, since the BMS corn cells used by Barry *et al.* in Example 5 cannot be regenerated, it is clear that Barry *et al.* would not have suggested to a scientist knowledgeable in the field in March of 1997 the production of a whole plant, let alone a whole soybean plant or seed with both glyphosate and sulfonylurea resistance transgenes.
7. I also provide the following information regarding independent experiments carried out on behalf of Monsanto Company relating to stacking of two glyphosate resistance genes in corn, tobacco and cotton.

8. CP4 and GOX are two genes evaluated by Monsanto Company in the 1990's for yielding glyphosate tolerance (resistance) in various crops. CP4 is a gene cloned from *Agrobacterium* encoding an EPSPS (5-enolpyruvyl shikimate 3-phosphate synthase) enzyme that is naturally insensitive to glyphosate. GOX (glyphosate oxidoreductase) was cloned from *Achromobacter* and encodes an enzyme that degrades glyphosate to AMPA (aminomethyl phosphonic acid) and glyoxylate. These two glyphosate herbicide tolerance traits were transformed into plant species and evaluated for tolerance and fertility to field rates of glyphosate.
9. The following table provides a summary of extended leaf height (cm) data in 1996 from corn transformed with CP4 and GOX (designated Jeremy, Leah, and Acrostic) and CP4 only (Bonnie) after spraying with 128oz/A Roundup (left), 128 oz/A Roundup plus 200 mM threonine (T) and 200 mM isoleucine (I) (middle) and unsprayed.

	<u>128 oz</u>	<u>128 oz + I + T</u>	<u>unsprayed</u>
Jeremy	65.8	73.2	81.6
Leah	67.8	76.0	86.2
Acrostic	63.7	74.8	83.2
Bonnie	86.0	82.0	84.2

10. The results showed that CP4 x GOX corn plants (Jeremy, Leah, and Acrostic) were stunted from glyphosate spray relative to CP4 only (Bonnie) plants. The addition of GOX in corn therefore resulted in *reducing* glyphosate tolerance, which was unpredicted.
11. Corn crossing experiments with CP4 and GOX events were made as follows. Seven CP4 only events (designated Bonnie, Caleb, Ghana, Leah, Olivia, Sherri and Kappus) were crossed with a GOX only event (Eileen) and evaluated for glyphosate tolerance at 0.75 or 1.5 lb/a in two field trials in 1995. Out of 7 CP4 x GOX crosses, 4 showed greater injury

(or growth reduction), 2 showed comparable injuries and 1 showed less injury than CP4 alone.

12. I further provide the following evaluation of injury or male sterility from glyphosate sprays in crosses of tobacco plants containing GOX or CP4.
13. GOX only lines showed good fertility and no injury (10 on a scale of 1-10) to 0.4 lb/a of glyphosate. At higher rates all lines showed initial vegetative damage with slight recovery after 28 days but remained fertile. CP4 only lines showed no to slight injury (7-9) with increasing doses of glyphosate (0.75 to 3 lb/a) but male sterility at high rates. Crosses of CP4xGOX showed slightly higher vegetative injury even at the 0.75 lb/a rate and lower male sterility than the GOX only lines.
14. I also provide the following summary of injury data (scale of 1-10) from 1988-1996 in cotton transformed with CP4 and/or GOX and sprayed with either 64 or 128 oz glyphosate/ac.:

pMON	trait	N	Inj 64 oz (1-10)	stdev	Inj 128 oz (1-10)	stdev
17110	CP4	12	9.2	2.0	8.6	2.7
17131	CP4	4	9.8	0.5	9.5	0.6
17138	GOX	4	9.0	0.0	7.8	2.1
17136	CP4/GOX	28	7.8	2.4	7.2	2.8

15. These results show that many events from the CP4 only constructs (pMON17110 and 17131) produced little injury when sprayed with glyphosate at either 64 or 128 oz/a (1.5 or 3.0 lb/a). Events from the GOX only construct (pMON17138) showed comparable to slightly higher injury than the CP4 only events. In comparison, the CP4/GOX events

showed the most injury compared to either CP4 or GOX only events. This is opposite of what would be predicted.

16. From the above data, I conclude that the performance of stacked glyphosate resistance genes in corn, tobacco and cotton is unpredictable for the following reasons. In corn, the addition of the GOX gene to a CP4-containing variety reduced the resistance of the tested corn to glyphosate over plants having CP4 alone, whereas addition of the GOX gene would have been predicted to increase glyphosate resistance. Additionally, in tobacco, CP4 only plants showed vegetative tolerance with insufficient male fertility, whereas GOX lines showed vegetative tolerance and good fertility. Crossing CP4 and GOX tobacco lines improved male fertility slightly but still less than that of GOX only lines. The inability of GOX to fully restore male fertility in CP4 lines of tobacco was unexpected and not predicted. In cotton, the stacking of CP4 and GOX in cotton actually reduced tolerance to glyphosate.
17. Based on the above data, I conclude that stacking of the glyphosate resistance genes CP4 and GOX does not provide predictable results, since plants with the two stacked genes were often less resistant to glyphosate than plants with either gene alone. While both transgenes in these studies conferred tolerance to the same herbicide, the transgenes did so by different modes of action. This confirms the general unpredictability of herbicide resistance when combining more than one herbicide resistant transgene. Given these results, the fact that soybean plants stacked to contain transgenes conferring glyphosate and glufosinate herbicide tolerance are effective to provide tolerance to both herbicides with an acceptable yield is therefore surprising and unexpected.

18. I hereby declare that all statements made of my own knowledge are true and all statements made on information are believed to be true and further that the statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment or both under § 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of this application or any patent issued thereon.

Date: 3/27/2009

Paul Feng

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